Remarks

Claims 26 and 35 have been amended to make the reference to "injection" part of the preamble to the composition portion of the claim. It is respectfully submitted that with this amendment these claims are no longer indefinite. Claim 47 has been amended to be dependent from Claim 36 rather than 13. It is respectfully submitted that with this amendment the claims are no longer indefinite.

Claims 26 to 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lewis (U.S. Pat. 5,288,496) in view of Herbert et al. (U.S. Pat. 5,654,008) and Okada et al. (4,652,441). Applicant respectfully traverses this rejection. Applicant's' composition comprises a first component contained in a delivery vehicle capable of immediately releasing said biologically active composition upon implantation in an animal body. Lewis discloses as his invention a formulation containing a growth promoter dispersed in a micro-particle matrix material (col. 3, l. 63-65). The composition of Lewis is described as being micro-particles (col. 3, l. 41). Lewis further states that "by an appropriate selection of polymeric materials a micro-particle formulation can be made such that the resulting micro-particles exhibit both defusional release and biodegradation release properties." (col. 4, l. 36-40) Lewis also discloses that the micro-particles can be mixed by size or type to provide for a multi-phasic delivery, and that other agents may be added either in micro-particle form or in conventional unencapsulated form where they are "blended with the growth promoter and provided to an animal by the method of the invention." (col. 6, l. 42-54)

In contrast, applicant's invention requires that the components are maintained as discrete, separate physical entities. The distinction between the mixture proposed by Lewis and the discrete composition of applicant is important in the practical dosing of animals. The composition of Lewis provides a fixed ratio between the growth promoter and the other drug selected. On the other hand, the composition of applicant allows for variability in the ratio since the number of pellets of each type selected for implantation can vary depending upon the needs of the particular animal.

Herbert discloses multi-phasic drug delivery systems (col. 17, l. 46-65) but once again they are continued with a primary active ingredient. Accordingly, Herbert adds nothing to the disclosure of Lewis. Okada discloses sustained release compositions (col. 4, l. 11-54) but does not disclose the addition of immediate release pharmaceutical compositions to a prolonged release composition. It is respectfully submitted that Lewis, Herbert and Okada, alone or in combination, do not render applicant's invention obvious.

Claims 26-30, 33, 36-40, 43-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stevens et al.

Stevens does disclose the injection of different types of pellets. However, Stevens does not disclose the injection of pellets designed to provide immediate release and long-term release of the same drug product. Instead, Stevens is concerned with the problems of infection caused by the injection of pellets. After describing the method of injecting pellets into an animal's ear, Stevens goes on to describe the main purpose of his invention:

> It is virtually impossible in such situations to provide a sterile injection site on a single animal or to prevent transfer of infected microbes from one animal to the next on the injecting needle. Further complicating the matter is that other procedures may be occurring at the same time as the implanting operation while the animal is confined, such as ear tagging, branding, veterinary inspections or procedures, or the like, which may further excite the animal and make injecting and disinfecting difficult. It is not unusual to even have manure at the injection site.... Consequently, bacteria introduced into the implant site, either during the delivery of the implant or thereafter may cause an infection at the site. (col. 1, l. 61; col. 2, l. 26)

Stevens states the principle objects and advantages of his invention as providing an antibiotic pellet system which permits localized sustained antibiotic release at the injection site in order to combat infection in or around the site of injection. (col. 3, l. 34-38). It is respectfully submitted that nothing in Stevens discloses a formulation containing an immediate release and a sustained release form of the same drug.

Claims 1, 6-10 13, and 17-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rickey et al. Rickey discloses (col. 13, l. 29-42) that the micro-particles may contain one or more active agents and that they may be mixed by size or by type so as to provide multi-phasic delivery. Rickey further discloses that other drugs in unencapsulated form may be blended with the primary active agent. However, Rickey does not disclose that a sustained release form of a drug and an immediate release form of the same drug may be combined in separate delivery vehicles.

Claims 26-30, 33, 36-40, 43-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Guittard et al. Guittard discloses an osmotic drug delivery device that has a drug agent in the wall of the tablet and an osmotic drug delivery device inside the tablet. The drug in the wall may optionally be the same drug or a different drug from that in the osmotic drug delivery system (col. 5, l. 3-5).

Applicant respectfully notes in that the claims, as amended, do not include osmotic drug delivery devices as one of the methods for delayed release. Applicant further notes that the osmotic pressure drug delivery system of Guittard requires the presence of a considerable amount of liquid to drive the osmotic drug release system. Accordingly, the Guittard tablets are generally swallowed and release their drug product during passage through the gastrointestinal system. These tablets are poorly suited for use as an implanted drug delivery system.

It is respectfully submitted that none of the cited references disclose applicant's invention. It is further submitted that when the references are taken alone or in combination none of the references suggest applicant's invention. Accordingly, applicant believes that the claims of this case are in condition for allowance and respectfully solicits such action.

Respectfully submitted,

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Version with Markings to Show Changes Made to Amended Claims

Applicant hereby amends Claim 26 as follows:

26. (TWICE AMENDED) An implant composition, suitable for implantation in an animal body by injection, comprising:

(a) a first component comprising a biologically active composition contained in a first delivery vehicle capable of immediately releasing said biologically active composition upon implantation in an animal body and which is selected from the group consisting of encapsulants where the coating wall material is highly soluble in body fluids, porous or freeze-dried solid compositions, solid tablets or pellets containing a disintegrating agent which causes the solid tablet or pellet to rapidly break down when in body fluids, solid tablets or pellets containing said biologically active material in fine or micronized particle sizes and mixtures thereof; and

(b) a second component comprising the same biologically active composition as in component (a) contained in a second delivery vehicle capable of releasing said biologically active composition on a sustained basis upon implantation in an animal body and which is selected from the group consisting of encapsulated solutions or suspensions, biodegradable solid substances, conventional tablet/pellet ingredients, conventional tablet/pellet ingredients coated with a polymeric membrane to control release, conventional tablets or pellets containing said biologically active material having large particle sizes, matrix-tablets based on gel-forming excipients, matrix-type systems based on non-biodegradable polymers, membrane-type systems based on non-biodegradable polymers, matrix-type systems based on biodegradable polymers, matrix-type systems implant based on lipidic excipients, and mixtures thereof[;].

[wherein said implant composition is implanted in an animal body by injection.]

Applicant hereby amends Claim 35 as follows:

35. (AMENDED) The implant of claim 34, suitable for administration by a single injection, consisting essentially of one to four pellets of type (a) and four to six pellets of type (b). [which is administered by a single injection]

Applicant hereby amends Claim 47 as follows:

47. (AMENDED) The method of Claim [13] 36 wherein step (2) comprises a single injection.